

Bicuspid Aortic Valve Prevalence in Adults to whom Echocardiography was Performed: Result of Single Center Experience

Ekokardiyografi Yapılan Erişkinlerde Biküspit Aortik Kapak Sıklığı: Tek Merkez Deneyim Sonuçları

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Abstract

Purpose: Bicuspid aortic valve (BAV) is the most common congenital cardiac anomaly in adults. Although there is some publication about the frequency of BAV, there is limited data about BAV in adult patients in our country. The aim of our study was to determine the prevalence and echocardiographic characteristics of BAV patients who underwent echocardiography.

Materials and Methods: To determine patients with BAV, three and half year echocardiographic data in our adult cardiology clinic was retrospectively examined in this retrospective study. Demographic features and laboratory findings were also obtained from hospital record. Student t-test, chi-square test and multivariate linear regression analyses were used for the statistical analysis.

Results: Among 52742 patients, BAV prevalence was found to be 4.4 (n=235) in 1000 patients. The median age of BAV patients was 46.4±17.6 years and 159 (67.7%) patients were male. Ascending aorta dilatation was found in 117 (51%) patients with BAV. BAV patients with aortic dilatation were significantly older (53.9±14.9 vs. 39.3±17.1, p=<0.001, respectively). Male gender were frequently seen in patients with aortic dilatation as compared without (%73.5 vs. %60.7; p= 0.039, respectively). Sixty-five (27.7%) of the BAV patients had aortic stenosis and echocardiographic graded as mild in 36 (15.3%), moderate in 20 (8.5%) and severe in 9 (3.5%) patients. Aortic regurgitation was observed in 185 (78.7%) out of the BAV patients and echocardiographic graded as mild in 144 (61.3%), moderate in 27 (11.5%) and severe in 14 (6.0%) patients.

Conclusion: The prevalence of BAV diagnosed by echocardiography at the adult cardiology clinic was 0.44%. Additionally, it was found that male gender and age were the most significant parameters associated with aortic dilatation. (**Sakarya Med J 2016, 6(3):146-151**)

Keywords: aortic regurgitation, aortic stenosis, bicuspid aortic valve

Öz

Amaç: Biküspit aortik kapak (BAK) en sık görülen konjenital kalp anomalisidir. BAK sıklığı ile ilgili bazı yayınlar bulunsa da, ülkemizdeki erişkin hastalardaki BAK sıklığı ile ilgili veriler kısıtlıdır. Çalışmamızın amacı, kliniğimize başvuran hastalardaki BAK sıklığının ve ekokardiyografik özelliklerinin belirlenmesidir.

Yöntem: Bu retrospektif çalışmada, BAK hastalarını bulabilmek için erişkin kardiyoloji kliniğimizde üç buçuk yıllık ekokardiyografi verileri geriye dönük olarak incelendi. Demografik özellikleri ve laboratuvar bulguları hastane kayıtlarından elde edildi. İstatistiksel analiz için student t-testi, ki-kare testi ve çoklu doğrusal regresyon analizi kullanıldı.

Bulgular: 52742 hasta içinde, BAK yaygınlığı 1000 hastada 4.4 (n=235) olarak bulundu. BAK hastalarının yaş ortalaması 46.4±17.6 ve hastaların 159 (67.7%)' u erkekti. BAK hastalarının 117 (%51)' sinde asendan aort dilatasyonu tespit edildi. Aort dilatasyonu olan BAK hastaları, olmayanlara göre anlamlı derecede daha yaşlıydı (sırasıyla 53.9±14.9 ve 39.3±17.1, p=<0.001). Aort dilatasyonu olan hasta grubunda, olmayanlara göre daha sık erkek cinsiyetle karşılaşıldı. BAK olan altmış beş (%27.7) hastada aort darlığı saptanmış ve ekokardiyografik olarak 36 (%15.3)' sinin hafif, 20 (%8.5)' sinin orta ve 9 (%3.5)' unun ise ciddi olduğu görüldü. Hastaların %78.7'sinde aort yetmezliği saptanmış ve ekokardiyografik olarak 144 (%61.3)' ünün hafif, 27 (%11.5)' sinin orta ve 14 (%6.0)' ünün ileri olduğu görüldü.

Sonuç: Erişkin kardiyoloji kliniğinde ekokardiyografi yapılan hastalarda BAK yaygınlığı %0.44 olarak bulundu. Ayrıca aort genişlemesi ile ilişkili en önemli parametrelerin erkek cinsiyet ve yaş olduğu bulundu. (**Sakarya Tıp Dergisi 2016, 6(3):146-151**)

Anahtar Kelimeler: aort darlığı, aort yetmezliği, biküspit aortik kapak

INTRODUCTION

Bicuspid aortic valve (BAV) which is one of the most common congenital disorders affects about 1% of general population according to the foreign sources. It has been shown to be associated with important valvular diseases including aortic stenosis (AS) and aortic regurgitation (AR) and increased risk for endocarditis from young to the advanced ages. In addition, incidence of aortopathies such as ascending aortic dilatation, ascending aortic aneurysm and aortic dissection is seen to be increased in BAV patients. BAV patients must be lifelong followed up due to risk for development of valvular disease and/or aortopathies that require surgical interventions.¹⁻³ Although there are studies conducted in our country which report the prevalence of BAV as 0.046% in newborns and 0.8% in cadets, there is no data about its prevalence in the general population^{4,5}. In this cross-sectional study, we aimed to determine prevalence and echocardiographic features of BAV in patients admitted to the adult cardiology clinic and undergone echocardiography, and by this means to provide contribution to the data repository that will be constructed in our country about the prevalence of this disease.

METHODS

Patients' Characteristics

In this retrospective descriptive study, among 52742 patients, we reviewed 235 patients with an echocardiographic diagnosis of BAV who underwent clinically indicated transthoracic studies from March 2011 to August 2014 in Adult Cardiology Clinic. The inclusion criteria were documentation of BAV on transthoracic or transesophageal echocardiography. Lack of confirmation of bicuspid status was specified as the exclusion criteria. Furthermore, patients' age, gender and medical history were examined from the hospital recordings. The ethical committee of our hospital approved this study.

Echocardiographic Examination

In our clinic, echocardiographic assessment of patients is performed through total 7 devices with 5 Philips and 2 General Electric brands with patients in the left lateral decubitus position. At the routine examination, after two dimensional and M-mode examination using parasternal long-axis views; left atrium, measures of aortic annulus diameter, ascending aorta, left ventricular end diastolic diameter, left ventricular

end systolic diameter and left ventricular end diastolic wall thickness (septum and posterior wall) are recorded. While an ascending aortic diameter between 20 and 37 mm was deemed as normal value, ascending aortic diameter > 3.7 cm was considered as ascending aortic dilatation^{5,6}. Ejection fraction is calculated by obtaining the left ventricular volumes from the parasternal long-axis window with Teicholtz method or from apical two and four-chamber views according to the modified Simpson method. Routine assessment is carried out with color Doppler, pulse wave Doppler and continuous wave Doppler using proper echocardiographic windows. Diagnosis Bicuspid aortic valve is established considering:¹ only two cusps monitored in the systole and diastole on the parasternal short-axis views;² elliptical-shape orifice monitored in the systole, and³ doming motion of the thick cusp with restricted movement in the systole and the cusps showing eccentric closure line on the parasternal long-axis views. In case of doubts about the valvular structure or if further assessment is deemed necessary, transesophageal echocardiography is used. In our clinic, severity of AR and AS is specified as mild, moderate and severe in the echocardiography report based on the principles stated in the guideline by European Society of Cardiology⁷. Echocardiography reports are recorded using FileMaker Pro Runtime 5.0 v4 software.

Statistical Assessment

Quantitative variables were expressed as mean \pm standard deviation. Compliance of the data to normal distribution was tested with Kolmogorov-Smirnov test. Statistical analysis was performed on computer using SPSS for Windows 20 (IBM SPSS Inc., Chicago, IL). Chi-square test or Fisher's "exact" Chi-square test was used in the categorical data between two groups, while Student's-t test was used for comparison of the data showing continuity. Multivariate linear regression analyses for the endpoint of aortic dimension were conducted to determine which clinical and echocardiographic variables were significantly associated with aortic dimensions. P values < 0.05 were considered statistically significant.

RESULTS

BAV was identified in 235 (0.44%) of 52,742 patients who underwent echocardiography in our clinic in three and a half years. Mean age of the patients was 46.4 ± 17.6 with 159

(67.7%) of the patients were male. Demographic and echocardiographic characteristics of patients are shown in Table 1.

Table 1. Baseline characteristics of the study subjects

	Patients with bicuspid aortic valve n=235
Age, years	46.4±17.6
Male gender, n (%)	159 (67.7)
Hypertension, n (%)	68 (28.9)
Diabetes mellitus, n (%)	26 (11.1)
Atherosclerotic heart disease, n (%)	51 (21.7)
LDL, mg/dL	130.9 (38-586)
Triglyceride, mg/dL	181.2 (38-810)
Aortic stenosis, n (%)	
None	50 (21.3)
Mild	144 (61.3)
Moderate	27 (11.5)
Severe	14 (6.0)
Aortic regurgitation, n (%)	
None	50 (21.3)
Mild	144 (61.3)
Moderate	27 (11.5)
Severe	14 (6.0)
LV end-diastolic diameter, mm	47.6±5.9
Ejection fraction, %	62.2±7.9
Interventricular septum, mm	10.3±1.7
LV posterior wall, mm	9.9±1.4
Left atrial diameter, mm	34.2±5.2
Ascending aorta, mm	37.5±7.5
LDL - low-density lipoprotein; LV - left ventricular	

Ascending aortic dilatation was found in 51% (n=117) of patients having BAV (Table 2). In addition, numbers of male gender and hypertensive patients were statistically significantly greater in those with aortic dilatation (73.5% vs. 60.7%; p=0.039, 39.3% vs. 19.6%; p=0.001; respectively). No significant correlation was found between patients with and without ascending aortic dilatation in term of the severity of AR. There was no significant correlation between patients with and without ascending aortic dilatation in terms of the severity of AS, but the trend was observed to approach statistical significance (p=0.053). When echocardiographic parameters were examined; end diastolic diameter, left atrium diameter, interventricular septum and posterior wall thickness were

found to be statistically greater and ejection fraction statistically lower in patients with ascending aortic dilatation than in patients without (p=0.004, p=0.012, p<0.001, p<0.001, p<0.001; respectively) (Table 2).

Table 2. A comparison of demographic and echocardiographic characteristics according to the ascending aortic dilatation in patients with bicuspid aortic valve

	Ascending aorta <37 mm (n=112)	Ascending aorta ≥37 mm (n=117)	p value
Male gender, n (%)	68 (60.7)	86 (73.5)	0.039
Aortic stenosis, n (%)			
None	88 (78.6)	78 (66.7)	0.053
Mild	15 (13.4)	20 (17.1)	
Moderate	4 (3.6)	15 (12.8)	
Severe	5 (4.5)	4 (3.4)	
Aortic regurgitation, n (%)			
None	30 (26.8)	18 (15.4)	0.207
Mild	65 (58)	78 (66.7)	
Moderate	12 (10.7)	14 (12.0)	
Severe	5 (4.5)	7 (6.0)	
Age, years	39.3±17.1	53.9±14.9	<0.001
Hypertension, n (%)	22 (19.6)	46 (39.3)	0.001
Diabetes mellitus, n (%)	12 (10.7)	14 (12.0)	0.765
LDL, mg/dL	121.0 (43-586)	124.0 (38-300)	0.831
Triglyceride, mg/dL	151.0 (38-810)	146 (59-570)	0.510
LV end-diastolic diameter, mm	46.4±5.0	48.7±6.3	0.004
LV end-systolic diameter, mm	30.4±4.9	31.3±5.4	0.177
Ejection fraction, %	63.5±6.5	61.0±8.8	0.012
Interventricular septum, mm	9.7±1.7	11.0±1.5	<0.001
LV posterior wall, mm	9.3±1.3	10.5±1.3	<0.001
Left atrial diameter, mm	33.0±5.2	35.4±5.0	<0.001
LDL - low-density lipoprotein; LV - left ventricular *Ascending aorta measurements of six patients could not be obtained.			

When BAV patients were assessed in terms of aortic stenosis; 170 (72.3%) have no AS. Whereas mild AS was found in 36 (15.3%), moderate AS in 20 (8.5%) and severe AS in 9 (3.5%)

patients. There was no aortic regurgitation in 50 (21.3%) of BAV patients; while mild AR was found in 144 (61.3%), moderate AR in 27 (11.5%) and severe AR in 14 (6.0%) patients. In multivariate linear regression analysis performed; advanced age and male gender were found to be correlated with increase of the ascending aortic diameter (Beta=0.402, $p<0.001$; Beta=0.153, $p=0.011$; respectively). However, effect of hypertension did not reach to statistical significance (Beta=0.011, $p=0.875$). When AR and AS that may affect aortic diameter were included in the analysis; age and male gender were seen to protect their significance. However, effect of AR and AS did not reach to statistical significance (Table 3). In terms of other congenital anomalies, aortic coarctation was detected in five patients (4 females and 1 male), cor triatriatum in a male patient; left persistent superior vena cava in a male patient, non-compaction cardiomyopathy in a female patient and ventricular septal defect was identified in a male patient. One male patient had history of operation due to atrial septal defect and mitral cleft. One male patient had been diagnosed for aortic valve vegetation and advanced AR.

Table 3. Multivariate linear regression analyses performed to find out possible factors that may affect the diameter of the ascending aorta

Parameters	Beta	B	95% Confidence Interval		p value
			Lower Bound	Upper Bound	
Male gender	0.151	2.420	0.517	4.324	0.013
Age	0.392	0.169	0.108	0.231	<0.001
Hypertension	0.002	0.025	-2.312	2.361	0.983
Aortic regurgitation	0.021	0.112	-0.535	0.759	0.733
Aortic stenosis	0.117	1.096	-0.016	2.209	0.053

DISCUSSION

In this sectional study, prevalence of BAV was found as 0.44% with more common in male gender. There is not any study in our country reporting prevalence of BAV in adult population. In this respect, this is the first study conducted in our country showing prevalence and patients' characteristic of BAV. However, in a study by Kardeşoğlu et al., prevalence of bicuspid aortic valve was found as 0.8% (n=6) in echocardiographic screening of 710 final years cadets⁵. Prevalence of bicuspid aortic valve was found as 4.6 in 1000 in an echocardiographic

screening performed by Tutar et. al in 1,075 newborns. In addition, BAV prevalence was found to be higher in boy than in girl newborns (0.71% vs. 0.19%; respectively)⁴.

Despite bicuspid aortic valve is the most commonly seen congenital heart disease, its real prevalence is not known. In a large autopsy series by Larson and Edwards including 21,417 consecutive patients, prevalence of BAV was found as 1.37% (n=293), while no significant difference was found between the genders in BAV prevalence⁸. Pauperio et al identified BAV in 13 (0.65%) of 2,000 fresh cadavers all of which were obtained from male cadavers. In this study, six valves were functionally normal, while evidence of stenosis were found in 5 and regurgitation in 2 valves. The authors observed that aortic coarctation accompanied in 1 of 13 cases⁹.

Prevalence of aortic dilatation in BAV patients may vary among the studies depending on the limit value taken into account for the dilatation and the aortic area from which the measures were read. Prevalence of ascending aortic aneurysm has been reported as 7.5-59% if the measures were taken from the level of annulus, 16-78% from the level of sinus valsalva, 15-79% for the level of sinotubular junction and 35-68% in case of the measurement from level of proximal ascending aorta¹⁰⁻¹³. In our study, area of measure for ascending aortic dilatation was proximal ascending aorta, limit value was taken as 3.7 cm and prevalence of ascending aortic dilatation was found as 51.0% (n=117).

In the present study, patients with aortic dilatation were observed to be older than those having no dilatation and male gender was more common. Aortic dilatation in BAV patients is known to begin in the childhood period. Several factors such as hypertension, male gender and valvular disease have important role in dilatation of the aortic diameter. However, it has been demonstrated in many studies that age is the most important factor^{14,15}. In a study by Della Corte et al., aortic dilatation was found in 56% of patients younger than 30 and 88% in those older than 80 years old¹⁶. In our study also age and gender were correlated with aortic dilatation. However, considering other parameters any correlation could be found between hypertension and aortic dilatation. Since our study was retrospective, some hypertensive patients might be

omitted, weakening a possible correlation. Furthermore, the correlation between age and hypertension in a certain proportion could lead to this effect.

Two hypotheses are mentioned for the development of aortic dilatation in BAV patients. First, aortic dilatation may develop in BAV patients due to the hemodynamic burden caused by post-stenotic dilatation from high velocity jet related to AS or resulted from increased pulse volume due to AR. Second is the congenital aortic fragility in the aorta. Bauer et al. demonstrated that high velocity jet created by the stenotic valve compared to a normal valve in BAV patients results in further increased shear stress in the anterolateral part of the ascending aorta¹⁷. Yasuda et al. showed that no benefit could be provided in prevention aortic dilatation following aortic valve replacement due to AS or AR in BAV patients and the authors made interpretation of progressive aortic dilatation in BAV patients might be due to the primary aortic wall fragility rather than hemodynamic factors¹⁸. Della Corte et al. examined predictors of ascending aortic dilatation in 280 BAV patients. They examined the patients in three groups as small, normal and dilated aortic phenotypes (dilated aortic root or dilated ascending aorta) according to the aortic diameters. Aortic dilatation was seen in 83.2% of patients in that study. Based on multivariate analysis, age (maximal risk in 50-60 years old) and severe aortic stenosis were found to be predictors of aortic dilatation at the mid-ascending level¹⁶. Whereas in our study no significant correlation was found between the severity of AS and aortic dilatation, but the trend was observed to approach statistical significance.

LIMITATIONS

Despite this is the first study in Turkey investigating prevalence of BAV in adult population, it has some limitations. First, data of this study were retrospectively obtained from the echocardiography reports and hospital recordings. Second, since our study included the patients who admitted to the cardiology clinic and underwent echocardiography, it should be kept in mind that the results may not reflect general population. Third, adequate image quality is needed in order to diagnose BAV and to assess the valvular structure more clearly. Chan et al. investigated patients' characteristics which affect usability of transthoracic echocardiography especially for the

diagnosis of BAV in patients who will undergo aortic valvular surgery. While success transthoracic echocardiography was less for the diagnosis of BAV especially in female patients and calcified valves, the authors showed that age was not effective in diagnosis. They stated that echocardiography has high specificity and sensitivity in case of the patients with sufficient echocardiographic images¹⁹. In our study, diagnosis of BAV was established with transthoracic echocardiography in 27 (11%) patients due to insufficient echocardiographic images. Nevertheless, it should be noted that some patients might be omitted due to poor image quality. Finally, cusp features of the bicuspid valve and measures at the levels of sinus valsalva and sinotubular junction were not included in this article since they have not been recorded for all the patients. In addition, only proximal aortic diameter was assessed for ascending aortic dilatation and index measures could not be given since body surface areas of the patients were unknown.

CONCLUSION

According to this single center study examining the patient encountered in daily practice of cardiology, prevalence of BAV was found as 0.44% in the patients undergone echocardiography. This was the first study demonstrating prevalence of BAV and echocardiographic characteristics of the BAV patients in our country.

Conflict of interest:

None declared.

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